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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/393,652	09/10/99	SRIVASTAVA	P 8449-025-999

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EXAMINER	
VANDER VEGT,F	
ART UNIT	**PAPER NUMBER**
1644	9

DATE MAILED: 06/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/393,652	Srivastava et al
Examiner	**Art Unit**
F. Pierre VanderVegt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 2, 2001*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above, claim(s) *4, 5, and 21-31* is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3 and 6-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Claims 1-31 are currently pending in this application.

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-3 and 6-21, drawn to treating with HSP complexed with antigen, in Paper No. 8, filed April 2, 2001, is acknowledged. The traversal is on the ground(s) that it would not constitute a serious burden on the Examiner to search the inventions of both Groups I and II because they both relate to treatment of an individual with compositions comprising heat shock proteins (HSPS) and the searches would therefore overlap. This is not found persuasive because Group I is drawn to the treatment of the subject with HSPS which are "pre-complexed" with an antigen and therefore the immune response in the recipient would be guided by said antigen, while Group II is drawn to the treatment of the subject with an HSP not pre-complexed with any particular antigenic molecule. Therefore, the HSP in that individual would need to associate with a graft-specific antigen in the recipient in order to induce the desired tolerance. Alternatively, the non-complexed HSP of Group II could also pick-up antigens in the recipient which are not related to the grafted tissue at all and therefore have no bearing upon the recipient's response to the graft.

The requirement is still deemed proper and is therefore made FINAL.

A/21

2. Claims 4, 5 and 22-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Accordingly, claims 1-3 and 6-20 are the subject of examination in this Office Action. It should be noted here that claims 6-20, which overlap both groups I and II, are being examined here in the context of how the claims relate to the elected invention of Group I.

Claim Rejections - 35 35 U.S.C. § 112

3. Claims 1-3 and 6-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Briefly, the claims are drawn to the treatment or prevention of graft rejection by the administration of compositions which comprise heat shock protein(s) non-covalently complexed with antigen. The specification is not enabling for the claimed invention. First, the claims are drawn to the use of HSPS non-covalently complexed to "an antigenic molecule." There is no specificity whatsoever in the claims regarding the nature of the antigenic molecule. The claims read upon any molecule which can elicit an immune response in the recipient animal. It would not be predictable to a person of ordinary skill in the art at the time the invention was made that modulating the immune response to a completely unrelated antigen would be of any significance to graft retention. Further, the sole exemplification of the claimed method, as shown in Figure 1, utilizes only HSP complexes from the liver and skin of animals of the donor's allotype. Therefore, Applicant's own working example shows only the use of HSP complexes which would be expected to be antigenically related to the graft material. Also, Applicant's own example shows only the administration of complexes to subject animals prophylactically, 10 days prior to graft placement, however, the term "treatment" comprises the administration of complex to a recipient after graft rejection has already begun. While directed at the treatment of autoimmune disease, the disclosure of Tisch et al (U on form PTO-892) is relevant here. Tisch discloses that administration of antigen after pathogenic cells have been activated may have an exacerbating effect on a condition, rather than a tolerogenic one. Second, the exemplification of the claimed invention, as depicted in Figure 1, would not lead the artisan to reasonably predict that the claimed method would be efficacious in the prevention or treatment of graft rejection. It is not readily apparent from examination of the data presented that the claimed method provides results,

in terms of long-term graft survival, which are any better than controls. All of the control animals show nearly total graft failure by day 10 post-grafting. The majority of HSP-Ag complex treated animals also show a substantial level of graft failure as well at day 10. It is respectfully submitted that in the Examiner's own personal experience in the study of skin allograft survival (VanderVegt et al (V on form PTO-892)), that following the graft survival for only 10 days after placement is considerably short-term and does not provide sufficient predictive value regarding the long-term success of the procedure. Tables 1 and 2 of the reference clearly show that control grafts, which would be immunologically predicted to fail, can persist for more than the 10 days of Applicant's example. Further, the example in the instant specification discloses only the tracking of a single graft per experimental animal. This is not adequate level of control. There is potential for failure of any given skin graft in the experimental animal for a multitude of reasons including, but not limited to, failure to prepare an adequate bed for the graft on the recipient, failure to obtain the proper depth of the graft tissue (i.e., to thick or too thin) or abrasion of the graft by the animal on its environment or by other animals in the cage. Accordingly, it is respectfully submitted that the results would be more meaningful if each animal were to bear the test allograft in duplicate as well as a syngeneic control graft.

In view of the nature of the invention, the paucity of guidance provided by the instant specification, the limited working examples, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute.

4. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 3 is ambiguous and unclear in the recitation of "the antigenic molecule is not an alloantigen of the grafted cells..." Does the term mean that the antigenic molecule is the same

allotype as the graft (i.e., would not be an alloantigen to the donor) or that the antigenic molecule is foreign to the donor and may or may not be foreign to the graft recipient? Clarification is respectfully requested.

Conclusion

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

6. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2001 365-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
June 15, 2001

F. PIERRE VANDERVEGT
PATENT EXAMINER